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EXAMINER	
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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/799,291	URAIZEE ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 17-24* is/are rejected.

7)☒ Claim(s) *20 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 10/8/2007 has been entered into the record. Claims 16 and 25-27 have been cancelled. Claims 1-15 and 17-24 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Claim Objections

Claims 20 and 24 are objected to for the following informalities:

Claim 20 in line 6 "1000 mg/1" should be "1000 mg/L"

Claim 24 line 2 "resent" should be "present" and the claim should contain a period.

Rejections Withdrawn

The rejection of claims 25-27 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-13 and 15-24 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment to claim 1 and claim 22 and the cancellation of the claim 16.

The rejection of claim 25 under 35 U.S.C. 102(e) as being anticipated by Davis et al. US 4,863,731, 198 is withdrawn in view of the cancellation to the claim.

The rejection of claim 25 under 35 U.S.C. 102(e) as being anticipated by Williams et al. US 6,146,838, Nov. 14, 2000 filed March 18 is withdrawn in view of the cancellation to the claim.

The rejection of claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-13, 16-19, 21,26 and 27 under 35 U.S.C. 103(a) as being unpatentable over Bhogal et al US 4,808,404 1989 in view of Smith et al. Parasitology 1998 vo1.117: S113-S141 is withdrawn in favor of a new rejection set forth below.

The rejection of claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-15.16-19, 21,26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 in view of Smith et al. Parasitology 1998 vol. 117:s113-s141 is withdrawn in favor of a new rejection set forth below.

The rejection of claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-15 16-19, 21-24, 26 and 27 under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 in view of Smith et al. Parasitology 1998 vol. 117 :S113-S141 and Dibner et al US 6,344,340, 2002 (provisional application filed March 1, 1999) and Clark et al. PNAS vol. 93, p. 6825-6829, 1996 is withdrawn in favor of a new rejection set forth below.

The rejection of claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 11-13, 16-19, 21-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhogal et al US 4,808,404 1989 in view of Smith et al. Parasitology 1998 vol. 117:S113-s141 and Dibner et al US 6,344,340, 2002 (provisional application filed March 1, 1999) and Clark et al. PNAS vol. 93, p. 6825-6829, 1996 is withdrawn

The rejection of claims 1, 2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 8-10,11-13, 16-19, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhogal et al US

4,808,404 1989 in view of Smith et al. Parasitology 1998 vol. 117 :$113-$141 and Jensen et al US 2004/0248793, Dec. 2004 - provisional application dated Jun. 30, 2003 is withdrawn.

The rejection of claims 1,2, 3 in-part, 4, 5, 6 in-part, 7 in-part, 8-10,11-15 16-19, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 and Smith et al. Parasitology 1998 vol. 117 :S113-S141 in view of Jensen et al US 2004/0248793, Dec. 2004- provisional application dated Jun. 30, 2003 is withdrawn in favor of a new rejection set forth below.

Rejections Maintained

The rejection of claim 14 under 35 U.S.C. 112, second paragraph is maintained for reasons made of record in the previous action.

Applicants argue that the term "dosage unit" is definite because as stated in the specification the instant composition can be provided in units of doses in vials and that claim 14 is directed to how the composition is packaged.

Applicants' argument is carefully considered but not persuasive. The instant claim does not recite that the instant composition is packaged into doses or vials. Further how can the composition of claim 1 (from which claim 14 depends) further comprise one or more dosage unit? As written the metes and bounds of claim 14 is not clear and appropriate correction is needed to clarify the claim.

New Rejections

Claims 1-7, 11-15,17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 in view of Hutchins et al. US 2003/0143717 A1 Jul. 31, 2003 filed Aug. 29, 2002.

The claims are drawn to a composition comprising viable sporulated oocysts of at least one species of protozoa known to cause coccidiosis, a pharmaceutically acceptable carrier, diluent, or excipient, and at least one surfactant capable of preventing or reducing the aggregation of sporulated oocysts, wherein the composition is substantially free of bacterial contamination.

Evans et al teach a composition comprising viable sporulated oocysts of two or more *Eimeria* species (e.g. *tenella, acervulina, maxima)* known to cause coccidiosis, phosphate buffered saline wherein the oocysts have been treated with 50% sodium hypochlorite (p.6 lines 16-19), hence, said composition is substantially free of bacterial contamination (p.3 line 15, p. 4 line 9- 19, p. 6 line16-19, p. 6 line 31-33, p.7 line 3-8, p. 8 claim 8). The instant specification on p.41 paragraph 110 teach that sodium hypochlorite may be used at a concentration from about 1%-10% to sterile the oocysts. Evans teaches 50% sodium hypochlorite; therefore Evans concentration of sodium hypochlorite surpasses the instant range 1%-10%. Thus, both the instant composition and the composition of Evans are substantially free of bacterial contamination whether 1-10% or 50% sodium hypochlorite is used.

Evans et al teach that said composition of sporulated oocysts is used as a vaccine and injected into eggs. Evans et al also teach the preparation of said composition of sporulated oocysts and that it is stored under refrigeration until needed (p.6 lines 1-10) It is obvious that said composition at a point is exposed to air and eventually stored in a container (e.g. for the purposes of refrigeration) and that such a container will contain a cap or stopper. Evans et al teach said composition having a dose of sporulated oocyst ranging from 102 to 108 oocysts per dose. Said oocysts are previously treated with bleach therefore said composition is substantially free of bacterial contamination.

As to claims, 17-19, the claims are product by process claims. Claims 17-19 recite process limitations such as" wherein said bacterial contamination is removed by tangential flow filtration" or" wherein bacterial contaminants have been removed from said composition at one or more step (s) of production" "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe,* 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP chapter 2113, Product-by-Process claims. Thus, claims 17-19 are drawn to the composition and not to the processes recited in said claims. The sterile phosphate buffered saline in which said sporulated oocysts are stored comprises water. Evans et al teach that said

composition of sporulated oocysts is used as a vaccine against coccidiosis caused by Eimeria species.

Evans et al does not teach a surfactant in said composition capable of preventing or reducing the aggregation of sporulated oocysts.

Hutchins teach that Eimeria oocysts clump and that a surfactant such as 20 can be used to reduce clumping or reduce the likelihood of the oocyst forming clumps.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to add a surfactant such as Tween™ to the composition of Evans et al because Hutchins et al teach that Eimeria oocysts clump and that a surfactant such as Tween™ can be used to reduce clumping or reduce the likelihood of the oocyst forming clumps. Further, it would have been prima facie obvious to one of ordinary skill in the art that the use of a surfactant to reduce clumping will ensure that doses of composition of Evans et al contain the right number of oocysts. The composition of Evans and Hitch as combined meets the limitation of claim 20 because said composition comprises the following: 0% by weight of alkali metal dichromate (not more than about 0.8%), 0% chloramine by weight (not more than about 0.75%), 0% hypochlorite ion (not more than about 10ppm) and 0% hydrogen peroxide (not more than 1000 mg/L).

Applicants' arguments against Evans et al ('233 application) and the response.

Applicants argue : " To be "substantially free of bacterial contamination," as this term is used in claim 1 of the present application, the composition is free from bacterial contaminants, which include "live, virulent, and infectious, or life-less or non-virulent, including cellular debris derived from such extraneous contaminants." In this context, the "bacterial contaminants" are separated from the composition of claim 1. These bacterial contaminants are removed from the recited composition by tangential flow filtration of an aqueous medium containing the oocysts and the bacterial contaminants using a filter membrane having a pore size that does not allow the oocysts to enter, but that allows the bacterial contaminants to pass through. As a consequence, the composition of claim 1 is not only substantially free of live bacteria that can be killed by sodium dichromate, but is also substantially free of dead bacteria and cellular debris that are derived from the source and remain in a vaccine composition after chemical treatment.

Applicants' argument is carefully considered but is not found persuasive. The instant claims are drawn to a product i.e. composition of claim 1 and not to a process i.e. methods by which bacterial contaminants are used to remove said contaminants. Thus, Applicants arguments as to the methods by which the instant composition is made substantially free of bacterial contamination is not commensurate with the scope of the claims. For the same reasons Applicants arguments that the '233 application fails to disclose or suggest the use of a filter pore size small enough to prevent the sporulated oocysts from entering the pores but large enough to allow bacteria to pas through the pores is not commensurate with the scope of the instant claims. As mentioned supra, the claims are not drawn to a method of making the instant composition

wherein filters are used to remove bacteria contamination. These are process limitations whereas the claims are drawn to a composition.

Applicants argue that the oocysts composition of the '233 applications is exposed to Chlorox (to kill bacterial contaminants) and this Chlorox is removed by "repeated washings" and that no process is performed to ensure that bacterial contaminants are separated from the oocysts and that "repeated washings" would not remove substantially all bacterial contaminants. Applicants' argument is carefully considered but is not found persuasive. As mentioned above, the claims are not drawn to methods of preparing the claimed composition. Also, although "bacterial contaminants" is defined in the specification to include both live and dead bacteria (see specification p. 10 paragraph 30), the instant claims recite 'substantially free of bacterial contamination". "Substantially free of bacterial contamination" is defined in the specification as below the level that can create a pyrogenic reaction when a vaccine of the invention is administered to poultry (p. 10 paragraph 30). The instant claims do not teach the level of bacterial contamination that can create a pyrogenic reaction. There is no comparison of the pyrogenicity of the product of the prior art and that of the instantly claimed composition. Further, in this specification there is no teaching of reduced pyrogenicity as compared to the art or reduced pryogen content.

Further, the specification on p. 10 paragraph 30 states that " a composition is substantially free of bacterial contamination when no bacterial contaminants [live or dead] are visible upon microscopic examination of the composition wherein the detection limit is at least about 1,100 bacteria per mL" Thus, Applicants definition of "substantially free of bacterial contamination" allows for at least one live or one dead bacterium.

Further the methods of the '233 application are provide for substantial repeated washing and centrifugation to remove contaminants (see page 6 of Evans et al) and multiple agents having i inhibitory or killing effect for bacterial, viruses and fungal agents. Potassium dichromate is known in the art in this process to serve several purposes including its antibacterial, antifungal and antiviral agent.

Applicants' arguments allege a higher degree of purity of the instant composition however it provides no intrinsic or extrinsic evidence thereof. Applicants' statement of a purer preparation by tangential flow filtration is unsupported by documented evidence and is conjecture and ignores the repeated wash steps of Evans to remove the sanitizing agents etc. Evan et al teach multiple rounds of centrifugation and resuspension in deionized or distilled water or saline to remove these contaminants and sporulating agents. These multiple washing steps would remove non-viable contaminants. Applicant's arguments are not supported by the methods of Evans et al. Applicants have provided no side-by side comparison of the composition of the art and the instantly claimed composition and evaluated the purity thereof and the arguments are limited to conjecture. The arguments are not persuasive, there is no showing that the process of multiple washings, centrifugations and density gradient separation would not achieve the same final composition. Applicant argues the process limitation of tangential flow filtration, however, no intrinsic or extrinsic evidence is provided that the final product of the two compositions are different in alleged contaminants.

Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference

between the claimed product and the prior art product. *In re Marosi*, 710 F.2d 798,802,218 USPQ 289, 292 (Fed. Cir. 1983).

The instant claims are still unpatentable over Evans and Hutchins as combined.

Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 and Hutchins et al. Us 2003/0143717 A1 Jul. 31, 2003 filed Aug. 29, 2002 as applied to claims 1-7, 11-15,17-21 above further in view of Dibner et al US 6,344,340, 2002 (provisional application filed March 1, 1999) and Clark et al. PNAS vol. 93, p. 6825-6829, 1996.

The combination of Evans et al and Hutchins et al is set forth supra. Said combination does not teach 0.5X phosphate buffered saline (PBS) and gentamicin in their combined composition.

Dibner et al teach a composition of sporulated oocysts in PBS containing 30 microgram/mL gentamicin or other acceptable disinfectant (column 8 last sentence).

Clark et al teach a composition of protozoan parasites in 0.5X PBS (p. 6826 left column under immunofluoresence microscopy).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include gentamicin and 0.5x PBS in the composition of Evans and Hutchins et al as taught by Dibner et al and Clark et al because Dibner et al teach a composition of sporulated oocysts in PBS containing gentamicin wherein

gentamicin is used as a disinfectant and Clark et al teach a composition of protozoan parasites in 0.5X PBS and PBS is generally used in the art as a buffer/diluent.

Applicants' arguments and the response

Applicants' argue that claim 1 is not rendered obvious in view of either the '233 application or the Smith et al reference and that resort to either the '340 patent (Dibner et al) and Clark et al does not cure the defect in the Office's obviousness rejection.

This argument is carefully considered but is not persuasive. The combination of Evans and Hutchins is obvious over claim 1 as set forth and addressed above on p. 5. Applicants' traversal of the Smith reference is moot in view of the withdrawal of said reference.

Applicants' argue that nowhere do either of the '340 patent or Clark et al disclose or suggest a composition comprising sporulated oocysts and a surfactant that prevents oocyst aggregation.

This argument is carefully considered but is not persuasive. The combination of Evans and Hutchins and Dibner and Clark are obvious as set forth in the rejection above and said combination teaches a composition comprising sporulated oocysts and a surfactant that prevents oocyst aggregation and further comprises other components such as buffer (0.5X PBS) and disinfectant (gentamicin). The combination of Evans and Hutchins and Dibner and Clark teach all of the recited elements in claim 1.

Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al WO 96/40233, 1996 and Hutchins et al. Us 2003/0143717 A1 Jul. 31, 2003 filed Aug. 29, 2002 as applied to claims 1-7, 11-15,17-21 above further in view of Jensen et al US 2004/0248793, Dec. 2004- provisional application dated Jun. 30, 2003.

The claims are set forth supra. The combination of Evans et al and Hutchins et al (set forth supra) does not teach surfactant concentrations of from about 0.05 mg/ml to about 10 mg/ml or 0.05 mg/ml to 2.0 mg/ml or 0.1 mg/ml to 2mg/ml.

Jensen et al teach surfactant used for stabilizing a pharmaceutical composition wherein said surfactants are added in the amount form 0.005 to 5mg/mL or 0.01 to 3 mg/mL (p. 10 paragraph 128). Jensen et al further teach that surfactants include those agents, which protect against aggregation (p. 7 paragraph 86).

It would have been prima facie obvious to one of skill in the art, at the time the invention was made to use the concentration range of surfactants in the composition of Evans and Hutchins et al as taught by Jensen et al because Hutchins teach that Eimeria oocysts clump (or aggregate) and that a detergent such as Tween ^{TM} 20, decreases the likelihood of clumping other particulates and because Jensen teach different concentrations (0.005 to 5mg/mL or 0.01 to3 mg/mL) of surfactant that can be used to stabilize a composition and thus reduce aggregation. Further, one of skill in the art based on the teachings of Hutchins that Tween ^{TM} 20 reduces clumping of Eimeria oocysts and the concentration of surfactant used to prevent aggregation in a composition can reasonably apply said Tween ^{TM} 20 in said concentration and optimize the

concentration to arrive at the instant concentration ranges.

As to Applicants' argument that at most Jensen discloses certain types of polypeptide compositions can be stabilized by surfactant; Jensen specifically teaches that surfactant can be used to protect against aggregation and teaches ranges of concentration of surfactant sufficient to stabilize a protein composition. The instant composition of Evans and Hutchins as combined is comprised of oocysts which contain proteins. So it is reasonable for one of skill in the art to reasonably apply said Tween ^{TM} 20 in the concentration ranges disclosed by Jensen et al to reduce aggregation in the composition of Evans and Hutchins as combined and also optimize the concentration ranges to arrive at a concentration that reduces aggregation with an expectation of success.

Status of Claims

Claims 1-15, 17-24 are rejected. Claims 20 and 24 are objected to. No claims allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645